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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/533,895	09/26/1995	SUZANNE L. TOPALIAN	2026-4205	1007

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OFFICE OF TECHNOLOGY TRANSFER
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ROCKVILLE, MD 20852

EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	35

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/533,895	Applicant(s) TOPALIAN ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-67,69,70,72-75,77,78,80,81,83,84,86,87,89,90 and 94-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-67,69,70,72-75,77,78,80,81,83,84,86,87,89,90 and 94-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 1995* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Group and Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Amy DeCloux, Group Art Unit 1644, Group 1640, Technology Center 1600.

Response to Arguments

2. In view of the amendment filed 4-2-02 (Paper No.34) PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Election/Restrictions

3. Applicant's election of Group I which encompasses claims directed to peptides from the region containing amino acids 56-70 including peptides having the sequence ID NO:s 1-5 and single point mutants thereof, in Paper No. 34, filed 4-2-02 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

It is noted that applicant has amended and cancelled claims such that the remaining pending claims are all drawn to the elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

5. Claims 65 and 73 are objected to because of the following informalities: The recitation of the first word "The" in the first line of claim 65 should be replaced by the word "An" to be consistent with the other independent claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89 and 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims encompass an MHC class II immunogenic peptide, wherein said peptide comprises a 9 amino acid segment of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, (claims 64, 69, 72, 77, 80, 83, 86 and 89) or consisting of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, (claims 66 , 70, 74, 78, 81, 84, 87 and 90).

The instant specification describes immunogenic peptides consisting of SEQ ID NO:s 1-5, compositions thereof, and methods comprising said peptides. However, the instant disclosure of peptides consisting of SEQ ID NO:s 1-5, compositions thereof, and methods comprising said peptides, does not adequately describe the scope of the claimed genus of peptides, each of which encompasses a substantial variety of subgenera, for two reasons.

First, only a partial structure is recited the instant claims encompass an MHC class II immunogenic peptide that comprises only 9 of the 14 -15 residues of the amino acid sequence of SEQ ID NO:s 1-5. It is noted that Janeway et al (Molecular Immunobiology 1999, page 122) teaches that peptides recognized by class II restricted cells are at least 13 amino acids long and can be much longer. Therefore, several amino acids of the MHC class II restricted peptide are not described.

Second, since the peptide comprises a nonamer, said peptide can also encompass an indeterminate number and type of additional amino acids, in addition to the amino acids set forth in the recited SEQ ID NO:s 1-5. With the exception of peptides consisting of SEQ ID NO:s 1-5, there is no description of the required structural and specific immunogenic functional features of the wide range of peptides encompassed by the instant claims, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the peptides encompassed. Therefore, the structure of an MHC class II immunogenic peptide, wherein said peptide comprises a 9 amino acid segment of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, (claims 64, 69, 72, 77, 80, 83, 86 and 89) or from the group consisting of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, (claims 66 , 70, 74, 78, 81, 84, 87 and 90) is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus an MHC class II immunogenic peptide, wherein

said peptide comprises a 9 amino acid segment of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, (claims 64, 69, 72, 77, 80, 83, 86 and 89) or consisting of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, (claims 66 , 70, 74, 78, 81, 84, 87 and 90), without further description from the instant specification.

It is noted that though the claimed invention is directed to polypeptides and not cDNA, the principle of the following still holds for said polypeptides: a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Claims 72, 74 and 77-78 encompass the above peptides linked to an MHC Class II molecule, However, the instant specification only describes the human MHC Class II molecule of HLA-DR-BR 0401 as the presenting molecule for the peptides consisting of SEQ ID NO:s 1-5 (Figure 5 and page 11). The prior art does not teach that said peptides can be presented by any other MHC Class II molecule. Therefore, one of skill would not recognize from the disclosure that applicant was in possession of the genus molecules comprising the recited peptides and an MHC class II molecule, with the exception of describes the human MHC Class II molecule of HLA-DR-BR 0401, without further description from the instant specification.

8. Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89 and 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 64, 66, 69, 70, 72, 74, 77, 78, 80, 81, 83, 84, 86, 87, 89 and 90 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide that consists of a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, does not reasonably provide enablement for the instant claims that encompass an MHC class II immunogenic peptide, wherein said peptide comprises a 9 amino acid segment of a sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, (claims 64, 69, 72, 77, 80, 83, 86 and 89) or consisting of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, (claims 66 , 70, 74, 78, 81, 84, 87 and 90).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims encompass an MHC class II immunogenic peptide, wherein said peptide comprises a 9 amino acid segment of a sequence selected from the group consisting of

SEQ ID NO:1 and SEQ ID NO:2, (claims 64, 69, 72, 77, 80, 83, 86 and 89) or consisting of SEQ ID NO:3 or SEQ ID NO:4 and SEQ ID NO:5, (claims 66 , 70, 74, 78, 81, 84, 87 and 90).

The instant specification discloses peptides consisting of SEQ ID NO:s 1-5, 18-19 and 24, compositions thereof, and methods comprising said peptides, and peptides consisting of SEQ ID NO:s 18-19 and 24 . However, other than peptides consisting of SEQ ID NO:s 1-5, compositions thereof, and methods comprising said peptides, the instant specification does not provide adequate guidance and direction regarding how to make and use any immunogenic peptide comprising a 9 amino acid segment of a sequence selected from a group consisting of SEQ ID NOs:1 and 2, which encompasses a substantial number of peptides, for two reasons.

First, only a partial structure is recited the instant claims encompass an MHC class II immunogenic peptide that comprises only 9 of the 14 -15 residues of the amino acid sequence of SEQ ID NO:s 1-5. It is noted that Janeway et al (Molecular Immunobiology 1999, page 122) teaches that peptides recognized by class II restricted cells are at least 13 amino acids long and can be much longer. Therefore up to 10 additional undefined amino acids need to be added to the 9 amino acid segment for recognition by MHC Class II restricted T cells. Due to the comprising terminology, the instant claims encompass peptides larger than just the 14-15mer of SEQ ID Nos:1-5 peptide, wherein said peptides encompass an indeterminate number and type of additional amino acids, in addition to the amino acids set forth in the recited SEQ ID NO:s 1-5.

Second, SEQ ID NOs: 1-2 comprises several 9 amino acid segments. However, it appears that at least some of said segments may not retain the ability to bind MHC Class II. The instant specification discloses in Figure 7 that the third residue of SEQ ID NO:1 (residue 58 of Ty56-70) is an anchor residue. Yet a nine amino acid segment consisting of residues 7-15 of SEQ ID NO:1, (residues 62-70 of Ty56-70) would not include said anchor residue, and accordingly may not bind to the MHC Class II molecule

Therefore, with the exception of peptides consisting of SEQ ID NO:s 1-5, the instant specification provides insufficient guidance and direction regarding the required structural and specific immunogenic functional features of the wide range of MHC Class II immunogenic peptides encompassed by the instant claims, or of the conserved regions that would be critical for the recited immunogenic features . Therefore, it would require undue experimentation by one of skill in the art to predict the sequence of the additional amino acid residues that are to be included in the MHC class II restricted peptide without further guidance and direction form the instant specification.

Claims 86-67 and 89-90 encompass a method of preventing or treating melanoma comprising administering at least one peptide. The instant specification provides invitro data demonstrating the ability of peptides consisting of the amino acid sequences of SEQ ID NO:1-5 to stimulate in vitro TILs from patients. However, the instant specification discloses no examples of administration to a mammal of nay disclosed or recited peptide. Razzaque (Vaccine 19:644-647 (2001)) teaches on page 644 that tumor vaccines are therapeutic, unlike conventional vaccines for infectious diseases which are mostly preventative in nature. therefore, it would

require undue experimentation for one of skill to practice a method of preventing melanoma without additional guidance and direction from the instant specification. Furthermore, Rosenberg (Immunology Today 18(4):175-182 (1997)) teach that although tyrosinase (from which the recited peptides are derived) appears to be an antigen recognized on a variety of MHC molecules, only TILs restricted by HLA-A24 have been shown to mediate tumor regression in vivo(see entire article, especially page 178). Since Hla-A24 is a class I molecule, it would require undue experimentation for one of skill to use a pharmaceutical composition comprising any of the recited Class II peptides in a method of treating melanoma without further guidance and direction from the instant specification.

9. Claims 96-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims recite three derivatives of the immunogenic MHC Class II peptide consisting of SEQ ID NO:1. Said three derivatives are identified as SEQ ID Nos: 18, 19 and 24. However the instant specification discloses in Figure 6 that unlike SEQ ID Nos:1-5, said three derivatives are not recognized by CD4+ T cells as measured by GMCSF secretion by T cells co-cultured for 24 hours with peptide pulsed autologous transformed EBV B cells. Therefore it would require undue experimentation for one of skill to use the peptides recited in claims 96-97 without further guidance and direction from the instant specification

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 64-67, 69-70, 72-75, 77-78, 80-81, 83-84, 86-87, 89-90 and 94-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 92 is indefinite in the recitation of the phrase "wherein the Q at position 1 is absent" because it is not clear if position 1 is any other amino acid other than Q, or if there is no amino aid at said position.

B) Claims 64-67, 69-70, 72-75, 77-78, 80-81, 83-84, 86-87, 89-90 and 94-99 are indefinite in the recitation of "An isolated Major Histocompatibility Complex Class II immunogenic peptide" because it is not clear that any 9 amino acid segment of the sequences of SEQ ID NO:1 or SEQ ID NO:2 are comprised by a MHC Class II peptide. Perhaps inserting the word "restricted" between class II and peptide was intended.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 64 and 69 and 80 are rejected under 35 U.S.C. 102(e) as being anticipated by Kwon, US Patent 5,679,511, Issued 10-21-1997, filed 6-1-1992.

'511 teaches a sequence (SEQ ID NO:10) that comprises SEQ IDNO:1 and SEQ ID NO:2 of the instant application, Claim 80 is included because '511 teaches that said peptide is suspended in PBS, a pharmaceutical composition. Claim 69 is included because of the open language of comprising. Therefore the referenced teachings anticipate the claimed invention.

14. It is noted that the prior art does not teach a peptide consisting of the sequences of SEQ ID NO:1-5, 18-19 or 24.

15. No Claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Patrick J. Nolan

Amy DeCloux, PhD
Patent Examiner, Group 1640,
June 12, 2002

Patrick J. Nolan, PhD
Primary Patent Examiner, Group 1640,